

**Amendments to the claims:**

Certain claims have been amended and others canceled below without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in a continuation application.

The following listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of claims:**

1. (amended) A method of detecting whether a subject is predisposed to, or afflicted with, a pulmonary ~~disease~~ hypertension which comprises (1) obtaining a suitable sample containing bone morphogenetic protein receptor II or nucleic acid encoding same from the subject; and (2) detecting in the bone morphogenetic protein receptor II or nucleic acid encoding same ~~sample whether a bone morphogenetic protein receptor-II mutation which is not present~~ which is not present in wildtype bone morphogenetic protein receptor-II or nucleic acid encoding same,

wherein the presence of such a mutation indicates that the subject is predisposed, to or afflicted with, the pulmonary ~~disease~~ hypertension.

2. (amended) The method of claim 1, wherein the suitable sample ~~is comprises a nucleic acid sample, and the mutation is detected in~~ a nucleic acid encoding bone morphogenetic protein receptor-II.

3. (amended) The method of claim 1, wherein the suitable sample ~~is one which~~ comprises a bone morphogenetic protein receptor-II polypeptide, ~~and the mutation is detected in the bone morphogenetic protein receptor-II polypeptide.~~

4. (amended) The method of claim 1, wherein the pulmonary ~~disease~~ hypertension is Primary Pulmonary Hypertension.

5. (original) The method of claim 4, wherein the Primary Pulmonary Hypertension is Familial Primary Pulmonary Hypertension.

6-50. (canceled)

51. (amended) A method of predicting an increased likelihood of a subject giving birth to twins or triplets which comprises:

- a) obtaining a suitable nucleic acid sample from the subject;
- b) detecting the presence of one copy of a ~~mutant~~ nucleic acid which encodes a mutant bone morphogenetic protein receptor-II polypeptide, thereby indicating that the subject is heterozygous for the ~~mutation~~ mutant bone morphogenetic protein receptor II,

wherein heterozygosity predicts an increased likelihood of the subject giving birth to twins or triplets.

52. (amended) A method of predicting an increased likelihood of a pregnant subject having a miscarriage ~~prior to giving birth to a child~~ which comprises:

- a) obtaining a suitable nucleic acid sample from the subject;

b) detecting the presence of two copies of a ~~mutant~~ nucleic acid, each of which encodes a mutant bone morphogenetic protein receptor-II polypeptide, thereby indicating that the subject is homozygous for the ~~mutation~~ mutant bone morphogenetic protein receptor II,

wherein homozygosity predicts an increased likelihood of the subject having a miscarriage ~~prior to giving birth to a child~~.

53. (withdrawn) A method of preventing and/or treating Familial Primary Pulmonary Hypertension in a subject which comprises introducing a nucleic acid encoding a wildtype bone morphogenetic protein receptor-II polypeptide operably linked to a promoter into a suitable cell under conditions such that the nucleic acid expresses the wildtype bone morphogenetic protein receptor-II protein so as to thereby prevent and/or treat Familial Primary Pulmonary Hypertension in the subject.

54. (canceled)

55. (withdrawn) A method of preventing and/or treating Familial Primary Pulmonary Hypertension in a subject which comprises administering to the subject an effective amount of a wildtype bone morphogenetic protein receptor-II polypeptide comprising consecutive amino acids having the sequence set forth in SEQ ID NO:2 to prevent and/or treat Familial Primary Pulmonary Hypertension in the subject.

56. (amended) A method of detecting whether a subject is either predisposed to, or afflicted with, Familial Primary Pulmonary Hypertension which comprises:

- a) obtaining a suitable nucleic acid sample from the subject; and
- b) detecting the presence of a (GGC)<sub>12</sub> trinucleotide repeat at positions corresponding to positions -928 to -963 in the 5' end of the subject's bone morphogenetic protein receptor-II gene,

wherein the presence of the trinucleotide repeat indicates that the subject is either predisposed to, or afflicted with, Familial Primary Pulmonary Hypertension.

57. (withdrawn) A method of screening for a compound capable of treating Familial Primary Pulmonary Hypertension which comprises:

- a) contacting a cell which expresses a mutant bone morphogenetic protein receptor-II with the compound; and
- b) determining whether the compound is capable of reversing the functional deficit present in Familial Primary Pulmonary Hypertension in the cell, wherein a reversal of the functional deficit in the cell indicates that the compound is capable of treating Familial Primary Pulmonary Hypertension.

58. (canceled)

59. (withdrawn) A method of obtaining a composition which comprises:

- a) identifying a compound capable of treating Familial Primary Pulmonary Hypertension by the method of claim 57; and
- b) admixing the compound so identified or a homolog or derivative thereof with a carrier.

60. (withdrawn) A transgenic non-human animal whose cells comprise a mutant nucleic acid which encodes a bone morphogenetic protein receptor-II polypeptide.

61-63. (canceled)

64. (new) The method of claim 2, wherein the mutation described relative to a difference from the sequence encoding wildtype bone morphogenetic protein receptor II set forth in SEQ ID NO:1 is selected from the group consisting of:

(1) a deletion of nucleotides having the sequence guanosine-guanosine-guanosine-guanosine-adenosine located at positions 1099-1103;

(2) a deletion of a thymidine nucleotide located at position 2579;

(3) a substitution of nucleotides having the sequence cytosine-thymidine-thymidine-thymidine located at positions 507-510 with nucleotides having the sequence adenosine-adenosine-adenosine;

(4) a substitution of a cytosine nucleotide located at position 2617 with a thymidine nucleotide;

(5) a substitution of nucleotides having the sequence adenosine-guanosine located at positions 690-691 with a thymidine nucleotide;

(6) a substitution of a cytosine nucleotide located at position 1471 with a thymidine nucleotide;

(7) a substitution of a guanosine nucleotide located at position 1472 with an adenosine nucleotide;

(8) a deletion of nucleotides having the sequence adenosine-thymidine-thymidine-thymidine located at positions 1248-1251;

(9) a substitution of a cytosine nucleotide located at position 994 with a thymidine;

(10) a substitution of a thymidine nucleotide located at position 295 with a cytosine nucleotide;

(11) a deletion of a guanosine nucleotide located at position 1097;

(12) a substitution of a guanosine nucleotide located at position 727 with a thymidine nucleotide;

(13) a deletion of an adenosine nucleotide located at position 1214;

(14) a deletion of nucleotides having the sequence adenosine-cytosine located at positions 2441-2442;

(15) a substitution of a cytosine nucleotide located at position 2695 with a thymidine nucleotide;

(16) a deletion of 21 nucleotides located at positions 189-209;

(17) a substitution of a guanosine nucleotide located at position 296 with an adenosine nucleotide;

(18) a substitution of a thymidine nucleotide located at position 250 with a cytosine nucleotide;

(19) a substitution of a guanosine nucleotide located at position 1040 with an adenosine nucleotide.

65. (new) The method of claim 3, wherein the mutation described relative to a difference from the wildtype bone morphogenetic protein receptor II sequence set forth in SEQ ID NO:2 is selected from the group consisting of:

(1) a mutation at a glutamic acid residue located at position 368 which causes the protein sequence thereon to be different from the wildtype bone morphogenetic protein receptor II sequence;

(2) a mutation at an asparagine residue located at position 861 which causes the protein sequence thereon to be different from the wildtype bone morphogenetic protein receptor II sequence;

(3) a substitution of a cysteine residue located at position 169 which causes premature termination of the protein sequence;

(4) a substitution of an arginine residue located at position 873 which causes premature termination of the protein sequence;

(5) a mutation at a lysine residue located at position 230 which causes the protein sequence thereon to be different from the wildtype bone morphogenetic protein receptor II sequence;

(6) a substitution of an arginine residue located at position 491 with a tryptophan residue;

(7) a substitution of an arginine residue located at position 491 with a glutamine residue;

(8) a substitution of a phenylalanine residue located at position 417 which causes premature termination of the protein sequence;

(9) a substitution of an arginine residue located at position 332 which causes premature termination of the protein sequence;

(10) a substitution of a cysteine residue located at position 99 with an arginine residue;

(11) a mutation at a proline residue located at position 366 which causes the protein sequence thereon to be different from the wildtype bone morphogenetic protein receptor II sequence;

(12) a substitution of a glutamic acid residue located at position 243 which causes premature termination of the protein sequence;

(13) a mutation at an aspartic acid residue located at position 405 which causes the protein sequence thereon to be different from the wildtype bone morphogenetic protein receptor II sequence;

(14) a mutation at a histidine residue located at position 814 which causes the protein sequence thereon to be different from the wildtype bone morphogenetic protein receptor II sequence;

(15) a substitution of an arginine residue located at position 899 which causes premature termination of the protein sequence;

(16) a deletion of consecutive amino acids having the sequence serine-threonine-cysteine-tyrosine-glycine-leucine-tryptophan located at positions 64-70;

(17) a substitution of a cysteine residue located at position 99 with a tyrosine residue;

(18) a substitution of a cysteine residue located at position 84 with an arginine residue;

(19) a substitution of a cysteine residue located at position 347 with a tyrosine residue.